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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,055	12/31/2003	Yoko Motoda	1686-0108P	8334

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EXAMINER	
AKHAVAN, RAMIN	
ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Applicant 08/23/04

Office Action Summary	Application No.	Applicant(s)	
	10/748,055	MOTODA ET AL.	
	Examiner	Art Unit	
	Ramin (Ray) Akhavan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 December 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/31/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of a preliminary amendment, filed 12/31/2003, amending the claims and the specification. Claims 1-13 are pending and under consideration in this action. It is noted that foreign language copies of the priority documents have been received (i.e. Japan 2001-201356, filed 07/02/2001 and PCT/JP02/06261, filed 06/24/2002).

Information Disclosure Statement

The information disclosure statement filed 12/32/2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. The references for which a copy was not found in the record have been crossed through.

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because Fig. 4 is not intelligible; characteristics or depictions disclosed therein are not discernible. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claim 2 would be grammatically correct if an article (e.g. "a") is inserted before "first PCR", as well as before "primer dimmers". Claim 10 is objected to because of the following informalities: the claim recites the term, "coding" when referring to a DNA sequence and its corresponding protein. It would be clearer if the term "encoding" were substituted for the term "coding". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. **Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

Base claim 1 is vague and indefinite and clearly is not directed to what applicants consider their invention. The claim as written is not distinguished by a first and second PCR reaction. However, the disclosure exclusively teaches that there is a first and second PCR reaction, i.e. the invention is directed to a two-step PCR method. (e.g. Spec. pp. 6-8, 16-17, 19-21, Fig. 1). As written, the claim is ambiguous and vague, as it does not particularly point out this feature of the invention, thus the claims' metes and bounds are indeterminable. The claim does recite that there are first, second and third double-stranded DNAs and a sense and anti-sense primer, but these limitations are not directed to separate PCR reactions or separate PCR solutions.

It logically follows that Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: that there is a first PCR reaction, the product of which is used in a second PCR reaction.

In addition, base claim 1 recites the terms, "5' terminal... " and "3' terminal region". It is unclear how the term "terminal" is to be interpreted in determining the claims' metes and bounds. In other words, the term "terminal" is vague, indefinite and open to interpretation (i.e. subjective). For example, it would be unclear as to how extensively second and third DNA fragments would have to overlap with the first DNA fragment.

Claim 1 also recites that the second DNA fragment comprises regulatory sequence for "transcription and translation of a gene". Generally nucleic acid structures affecting transcription and translation are distinct (e.g. upstream activation sequences versus sequences forming hairpins or ribosome binding sites for regulating translation). As written, it is unclear whether a single sequence is intended to function in both transcription and translation of a gene. Therefore, the claims' metes and bounds are indeterminable with respect to this limitation. It would be remedial to replace the conjunction "and" with "or" to indicate that the sequence can be either a transcription regulatory or a translation regulatory sequence.

Claim 2 recites the limitation "the reaction solution (second PCR solution)" and "(first PCR)". There is insufficient antecedent basis for these limitations in the claim. As noted above, base claim 1, nowhere, recites that there is a first and second PCR reaction or PCR solution. In fact, base claim one only refers to a single "reaction solution".

Claim 3 recites the term "first PCR" which does not have sufficient antecedent support. (See supra; indicating that base claim 1 does not contain limitations as to a first and second PCR reaction or solution). In addition, the term "first PCR" is insufficiently descriptive, because it is not clear in what context the limitation is to be interpreted (e.g. reaction, solution).

Similarly, Claim 4 recites the term "second PCR" which does not have sufficient antecedent support and is also vague and indefinite with respect to what context the limitation is to be interpreted in determining the claim's metes and bounds.

Claim 5 recites the term "the primer dimmers" which does not have sufficient antecedent support.

Claim 6 recites the term "first PCR" which does not have sufficient antecedent support. Furthermore, the term "first PCR" is insufficiently descriptive, because it is not clear in what context the limitation is to be interpreted (e.g. reaction, solution). In addition, the claim is vague and indefinite because it recites the phrase, "the first PCR is carried out using recombinant microorganisms... ". Does applicant mean that the PCR reaction is being carried out in microbes or in culture media that may/may not contain microbes, extracts and various buffers?

Claim 10 recites the phrase, "wherein at least one of the..." referring to the second and third DNA fragments. It is unclear how this limitation is to be interpreted in determining the claims' metes and bounds. For example, as written a fusion protein could have a tag peptide on both ends. It would be remedial to replace the phrase above with the term "either".

Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP

§ 2172.01. The omitted elements are: that the method involves using cell extract to effectuate protein expression.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Sheikh et al. (WO 97/46696; see whole document).

The claim is directed to a method of producing a protein in a cell-free or *in vitro* system using a DNA template. It is not relevant what is the source of the DNA template.

Sheikh et al. teach an *in vitro* method for protein synthesis using cell extract.

3. Claims 1-11 and 13 are rejected under 35 U.S.C. 102(e) as being anticipated by Endo et al. (US Pub. No. 2004/0121346 A1; see whole document).

In the interest of compact prosecution, notwithstanding the claim rejections under § 112, ¶ 2, the claims are interpreted as being directed to a method involving a two-step PCR process in

producing a DNA fragment. Furthermore, claim 13 is interpreted to read on any *in vitro* method of protein synthesis.

Endo et al. teach a method involving a two-step PCR process to construct transcription templates for protein expression. (e.g. Abstract). More particularly, a primer (Primer 1) hybridizes to the 5' end of a target DNA (Primer 2), where the primer contains a transcription regulatory sequence, i.e. SP6 promoter sequence. (e.g. Fig. 2; p. 10, ¶ 0164). In addition, the Primer 2 itself contains sequences overlapping with a third DNA fragment (cDNA). (e.g. Id.). Furthermore, additional primers (I-III) are used to the 3' end (i.e. anti-sense primers for the cDNA). (e.g. Id.). In addition, at least one of the primers contains a tag peptide (i.e. GFP gene). (Id.). The template plasmid DNA is at a concentration of 50 pg/ul, which falls within the range of 5 – 2,500 pmol/L. (e.g. p. 11, ¶ 0177). The PCR product from this reaction is subsequently used in a second PCR reaction. (e.g. p. 11, ¶¶ 0179; p. 13, ¶¶ 0204-0209). Furthermore, the templates thus produced, are used to synthesize proteins in a cell-free reaction using cell extracts. (e.g. p. 14, Example 3, ¶¶ 0215-0218). In addition, the primer concentrations are between 20 to 500 nmol/L. (e.g. p. 13, ¶¶ 0205-0206). The first PCR products are diluted from 10-100 fold for the second PCR reaction (e.g. p. 15, ¶¶ 0224, 0228-0229). The PCR products are run on an agarose gel and desalinated, which would intrinsically remove primers or primer dimmers. (e.g. p. 14, ¶¶ 0210-0212). In addition, the peptide tag can be a histidine tag for efficiently purifying the gene product. (e.g. p. 8, ¶ 0140; p. 9, ¶ 0147). In sum, Endo et al. anticipate the rejected claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ramin (Ray) Akhavan whose telephone number is 571-272-0766. The examiner can normally be reached on Monday- Friday from 8:00-4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ray Akhavan/AU 1636

GERRY LEFFERS
PRIMARY EXAMINER